Safety and Efficacy of Intravitreal Tissue Plasminogen Activator Injection and Expansile Gas Pneumatic Displacement of Submacular Hemorrhage: A Systematic Review and Meta-Analysis

Mohammad Karam[1,2] MBChB, Sarah Saram[3] MBChB, *Narvair Kahlar[4] MBChB, Abdulmalik Alsaif [5,6] MBChB MPH

1 Department of Ophthalmology and Visual Sciences, McGil University, Montréal, QC, Canada 2 AlBahar Eye Center, Ibn Sina Hospital, Kuwait City, Kuwait 3 Royal Wolverhampton NHS Trust, Wolverhampton, UK 4 Birmingham Midland Eye Centre, Birmingham, UK 5 Royal Eye Unit, Kingston Hospital Foundation Trust, London, UK 6 King Khaled Eye Specialist Hospital, Riyadh, KSA

INTRODUCTION

Submacular hemorrhage (SMH) is a serious complication of various retinal disorders, including AMD, polypoidal choroidal vasculopathy, and retinal arterial macroaneurysm, as well as ocular surgeries like vitrectomy. SMH, especially when >4 disc diameters and subfoveal, can cause significant visual loss and retinal pigment epithelium (RPE) degeneration if untreated. Management strategies typically involve pars plana vitrectomy (PPV) with or without recombinant tissue plasminogen activator (tPA) and anti-VEGF therapy. Alternatively, a minimally invasive approach using intravitreal tPA combined with pneumatic displacement has gained attention for its simplicity and lower cost. This study systematically reviews the safety and effectiveness of intravitreal tPA and pneumatic displacement for treating SMH.

AIM

To assess the safety and efficacy of intravitreal tPA and pneumatic displacement of submacular hemorrhage.

METHOD

- A pre- and post-intervention systematic review and single-arm meta-analysis was conducted in line with guidelines from the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 Consensus Statement.
- Three electronic databases and the grey literature were searched for any studies evaluating intravitreal tPA and pneumatic displacement in the setting of submacular hemorrhage.
- The primary outcome was the corrected distance visual acuity (CDVA).
- Secondary outcomes included the incidence of adverse events such as vitreous hemorrhage, retinal detachment, retinal pigment epithelial (RPE) tears and endophthalmitis.
- The random-effects model was used to calculate the pooled mean with 95% confidence intervals (CIs).

RESULTS

- Thirteen observational studies, totalling 502 eyes, were eligible.

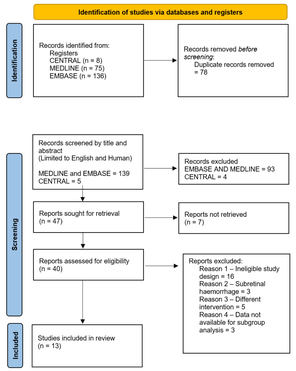


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of study selection.

- **CDVA** (SMD: 0.707, 95% CI: -1.036 to -0.379, P<0.05)
  - Preop mean: 1.180 logMAR
  - Postop mean: 0.788 logMAR

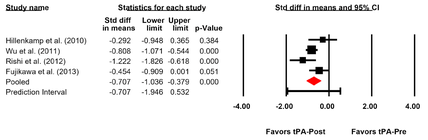


Figure 2: Forest plot of pooled estimate of standardized mean difference for best-corrected distance visual acuity (CDVA) in studies involving intravitreal tissue plasminogen activator (tPA) and pneumatic displacement in submacular hemorrhage (SMH).

- The incidence of **adverse events** with the use of tPA was low, including
  - Vitreous hemorrhage (Events rate: 0.112, 95% CI: 0.078 to 0.157)
  - Retinal detachment (Events rate: 0.057, 95% CI: 0.029 to 0.109)
  - RPE tears (Events rate: 0.075, 95% CI: 0.022 to 0.227)
  - Endophthalmitis (Events rate: 0.035, 95% CI: 0.010 to 0.114)

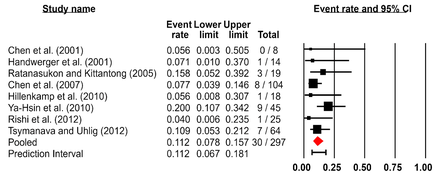


Figure 3: Forest plot of pooled event rates for vitreous hemorrhage in tPA and pneumatic displacement for SMH.

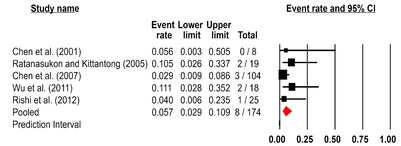


Figure 4: Forest plot of pooled event rates for retinal detachment in tPA and pneumatic displacement for SMH.

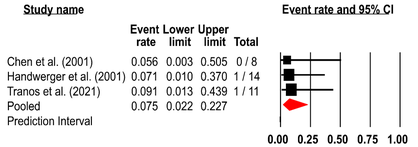


Figure 5: Forest plot of pooled event rates for RPE tears in tPA and pneumatic displacement for SMH.

CONCLUSION

In conclusion, the current systematic review and meta-analysis of intravitreal tPA and pneumatic displacement for SMH, which included a sample size of 502 eyes from thirteen observational studies, demonstrates significant improvements in visual acuity with a low incidence of adverse events. These findings suggest that tPA and pneumatic displacement are effective and safe treatments for SMH. Future studies should focus on conducting comparative analyses with other interventions and include long-term follow-up to better understand the sustained efficacy and safety of these treatments.